PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	Boyce
Serial Number	10/092,237
Filed	March 6, 2002
Confirmation No.	8680
Art Unit	1633
Examiner	Wehbe
Title	**SURGICAL DEVICE FOR SKIN THERAPY OR TESTING**
Attorney Docket No.	074057.7

Cincinnati OH 45202 July 8, 2009

DECLARATION OF STEVEN T. BOYCE, Ph.D.

1. I am the inventor in the referenced application.

2. I received my Doctor of Philosophy degree from the University of Colorado, in the field of molecular, cellular, and developmental biology. I have 34 years of experience in biomedical research, 26 of which are in the field of skin science research, the subject of this application.

3. Further to my April 23, 2009 Declaration, and as suggested by Examiners Wehbe, Woitach, Nguyen, and Kim at the June 3, 2009 personal interview in which I participated, I provide this Declaration to clarify the matrix, epidermal cell, and dermal cell components of my claimed device, and its resulting properties, features, and benefits.

Matrix

4. The matrix portion of my device is prepared from a collagen-containing fluid that is cast, frozen, and dehydrated. I have previously explained this preparation at p. 2 of my April 23, 2009 Declaration. The formed matrix contains no cells; it is acellular. The formed matrix is reticulated, it is not perforated.

5. My use of the term "reticulated" is consistent, throughout my specification, claims, and arguments, as describing a non-perforated, net-like structure. I note that some literature references use the terms

"reticulated" and "reticular" differently than I have used the term "reticulated". For example, the applied Krejci reference describes the deep dermis in natural skin as "reticular dermis", which is not how I use "reticulated". I thus respectfully assert that my use distinguishes over references that give the term "reticulated" a different meaning.

6. Cells are inoculated directly on my matrix. The matrix is impermeable to cells, but is permeable to liquids at the time of inoculation, which facilitates the deposition of a cell suspension on the surface of the matrix. If my matrix was perforated, the cells would pass through (i.e., pass into) the matrix thickness, and would not immediately form a lamination (i.e., covering) on the matrix.

Dermal Cells

7. Because my matrix is reticulated, not perforated, the dermal cells that are inoculated directly on the reticulated matrix cannot pass through. Instead, these dermal cells are captured or retained in the net-like structure of the reticulations, as on a filter. These dermal cells completely cover the matrix to immediately form a surface lamination, and completely attach to the surface in less than one day. I have schematically shown this at p. 3 of my April 23, 2009 Declaration.

8. For the reason explained in item 7, the dermal cell lamination layer is formed within a shorter time period than is possible using a perforated matrix.

Epidermal Cells

9. Epidermal cells are inoculated directly onto the lamination layer that was formed immediately when dermal cells were inoculated directly onto the reticulated matrix.

Device

10. This arrangement of a bottom matrix layer, a middle dermal cell layer, and an upper epidermal cell layer, schematically represented as

epidermal cells = second cell layer
dermal cells = first cell layer
matrix = substrate

does not include a basement membrane. Yet, under permissive conditions of incubation, my device spontaneously generates a continuous basement membrane as a natural bond between the epidermal cells and the dermal cell lamination layer (e.g., there are no isolated clumps or colonies of cells). My device forms a basement membrane in a reproducible, regulated, and predictable manner each time the device is prepared. It forms a basement membrane both before and after my device is transplanted into a

patient. Formation of a basement membrane is one property that verifies the device will have close analogy to the physiology and anatomy of uninjured, normal skin. The basement membrane promotes improved healing of open wounds by the device, and generates stable skin tissue to promote medical recovery.

11. The device enables epidermal cells to organize, establishing formation of a basement membrane. This was surprising and expected to me because the formation of basement membrane *in vitro* was not well understood at the time of this invention. This was not predictable to me, nor would it be predictable to a person of ordinary skill in this art, in my opinion, because the state of the art at the time of this invention was not sufficiently advanced. The formation of natural basement membrane, between dermal and epidermal cells that are in direct contact, is a clear distinction from my U.S. Patent No. 5,976, 878. In the '878 patent, the dermal cells and epidermal cells were not in direct contact. Rather, the lamination layer of the device in the '878 patent was acellular, was synthesized from the same collagen-containing polymer as the matrix, and provided only for rudimentary organization of an epidermal layer. The epidermal layer of the device in the '878 patent did not remain sufficiently attached to the matrix. Thus, my device has a composition which promotes more rapid and complete healing of skin wounds, both *in vitro* and *in vivo*. Images in Boyce et al., Skin Pharmacol. 1990, that the Examiners raised during the Interview, show such epidermal detachment from the polymer lamination, which compromises the capability of the device to accomplish rapid and complete healing.

12. This biological deficiency is corrected by the lamination of dermal cells that each of my claims recite.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the subject application or any patent issued thereon.

8 July 2009
Date

Steven T. Boyce, Ph.D.

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